

Assessment of The Quality of Life of Patients with Diffuse Toxic Goiter Against The Background of Drug Therapy and Surgical Treatment

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DOI : <https://doi.org/10.61796/jmgcb.v2i4.1208>



Sections Info

Article history:

Submitted: January 29, 2025
Final Revised: January 29, 2025
Accepted: January 30, 2025
Published: January 31, 2025

Keywords:

Diffuse toxic goiter
Endocrine ophthalmopathy
Thyrotoxic heart
Quality of life questionnaire SF-36

ABSTRACT

Objective: This study aims to evaluate the quality of life in patients with diffuse toxic goiter (DTG) undergoing drug therapy and surgical treatment. It also seeks to identify key predictors of complications associated with DTG. **Methods:** The study involved patients diagnosed with DTG, assessing the prevalence of subclinical and manifest thyrotoxicosis. The analysis focused on the impact of disease duration on complications such as thyrotoxic heart disease, endocrine ophthalmopathy, and toxic hepatitis. Additionally, the quality of life was compared between patients receiving thyroidectomy and those undergoing drug therapy with thyreostatics. **Results:** Findings indicate that DTG is more prevalent in women than men. Among the patients, subclinical thyrotoxicosis accounted for 66.7%, while manifest thyrotoxicosis was 33.3%. Disease duration was a critical factor in the progression of complications. Patients who underwent timely thyroidectomy exhibited better quality of life outcomes. Physical functioning improved by 23%, while emotional functioning, mental health, and social functioning increased by 40.7%, 22.5%, and 30.7%, respectively, compared to those receiving drug therapy. **Novelty:** This study highlights the significant role of thyroidectomy in improving the quality of life for DTG patients compared to drug therapy. It also emphasizes the predictive value of disease duration in the development of DTG-related complications, contributing to better clinical decision-making.

INTRODUCTION

Diffuse toxic goiter or Graves' disease is one of the most common thyroid diseases and the most clinically significant thyroid pathology, occurring in 0.5-1.5% of the population. It has been found that in iodine-deficient regions, which includes the Republic of Uzbekistan [1], the prevalence of Graves' disease is higher compared to iodine-sufficient regions. It should be noted that currently there is an increase in morbidity and an increase in the incidence of severe forms of pathology. At the same time, the literature covering pathophysiologic mechanisms of Graves' disease and its clinical manifestations is insufficient for a more complete understanding of this problem by students in residency training. Timely diagnosis of Graves' disease is often difficult due to the nonspecific nature of the clinical picture. In the absence of treatment, the disease is accompanied by severe cardiovascular disorders that can cause disability and death [2], [3], [4], [5], [6], [7], [8], [9], [10], [11].

Graves' disease is a systemic autoimmune disease characterized by diffuse thyroid lesions with the development of thyrotoxicosis syndrome. Graves' disease affects about 1% of the population, its prevalence is higher in iodine-deficient areas. Women suffer 10 times more often, the greatest risk of developing Graves' disease is in young and middle

age, in 20-40 years, which is generally characteristic of autoimmune pathology. The etiology of Graves' disease is unknown, at the moment we can only talk about the factors that provoke its development: - genetic predisposition; - stress; - infections; - smoking; - environmental factors [4], [1], [3].

Of the synthesized thyroid antibodies, the main importance belongs to antibodies to the TS receptor, which have a TSH-like stimulating effect, but longer than that of thyrotropin. These antibodies mimic the effect of thyroid hormone, which leads to hyperproduction of TH and proliferative process in the thyroid [12].

It is considered to be a disease that develops predominantly in women. The number of men suffering from Graves' disease not so long ago did not exceed 10% of the total number of patients [13]. However, in the last decade there has been an increase in the incidence of men with Graves' disease. The relative rarity of the disease is associated with late diagnosis - at the stage of complications from the cardiovascular system, when thyrotoxic therapy and subsequent surgical treatment are not effective enough [11]. Thyrotoxicosis, most often caused by Graves' disease, can lead to premature mortality if inadequately treated. There is no consensus on which of the three available treatment options-antithyroid drugs, radioactive iodine, and surgery-is better and their impact on patients' quality of life.

The aim of the study is to evaluate the quality of life of patients depending on the therapy received.

RESEARCH METHOD

General clinical investigations included assessment of endocrine status, general blood and urine analysis, electrocardiography (ECG), biochemical blood parameters - blood sugar, ALT, AST. We collected detailed anamnestic data of patients (the first symptoms that appeared in patients, the time of the first visit to doctors, the time of diagnosis, applied methods of treatment).

Endocrine status included the study of complaints, patient history, objective examination data, and thyroid function.

All patients included in the present study used immunoenzymatic method of analysis: determination of thyroid hormone (TSH), free triiodothyronine (fr.T3), free thyroxine (fr.T4) blood levels, immunologic markers - antibodies to thyroperoxidase (TPOAb) and antibodies to TTH receptors blood (TRAb).

The hormones were determined by serum blood using reagents of HEMA company (Russia). Reference values for TSH were 0.3-4.5 MED/L, for fr.T3 2.0-4.2 pg/mL, for fr.T4 - 8.9-17.2 pg/mL, TPOAb - 0-30ME/L, TRAb - 0-1.49 ME/L.

Instrumental methods of research included: ultrasound of thyroid gland on Voluson S6/S8 device with 7.5-12 transducer. On the basis of ultrasound data the volume of thyroid gland was calculated, blood flow and the presence of nodular masses were evaluated. Total thyroid volume was calculated by multiplying the length, thickness, width of each lobe, the obtained result was multiplied by the coefficient 0.479 (WHO

Recommendations 1994). The thyroid volume in women up to 18cm³ and in men up to 25cm³ was taken as normal values.

The SF-36 questionnaire [14], [15], [16], [17], [18], [19] was used to study the quality of life (QOL) in patients with Graves' disease, which reflects patients' satisfaction with their physical and mental state, social functioning, as well as self-assessment of pain syndrome severity. Total scores were determined for 8 parameters: physical functioning, role functioning, pain intensity, general health, vitality, social functioning, emotional functioning, and psychological health. The questionnaire was constructed in such a way that a higher score reflects a higher level of QoL.

The following indicators were quantified: physical functioning, which reflects the extent to which health limits the performance of physical activities such as self-care, walking, climbing stairs, carrying heavy loads, bending, as well as the tolerance of significant physical exertion; the impact of physical condition on role functioning (work, performing everyday activities); pain intensity and its impact on the ability to engage in everyday activities, including domestic and non-domestic work; general health status - assessing the ability to perform activities of daily living; and general health status - assessing the ability to perform activities of daily living, including domestic and non-domestic activities.

Statistical Analysis

The data obtained in the study were subjected to statistical processing on a Pentium-IV personal computer using Microsoft Office Excel-2003 software package, including the use of built-in functions of statistical processing. The methods of variation parametric and nonparametric statistics were used with calculation of arithmetic mean of the studied index (M), mean square deviation (s), standard error of mean (m), relative values (frequency, %), statistical significance of the obtained measurements when comparing mean values was determined by Student's criterion (t) with calculation of probability of error (P) when checking the normality of distribution (by the kurtosis criterion) and equality of general dispersions (F - Fisher's criterion). The level of reliability $P < 0.05$ was taken as statistically significant changes.

RESULTS AND DISCUSSION

The study was conducted in the department of 2-therapy and endocrinology and consultative polyclinic of 3-clinic of Tashkent Medical Academy. Fifty-seven patients with Graves' disease, of whom 38 women (66.7%) and 19 (33.3%) men prevailed.

Table 1. Age-sex composition of the surveyed.

	Number		Average age
	Abs	%	
Women	38	66,7	41,3±4,73
Men	19	33,3	37,9±5,29
Total	57	100	

The mean age of the patients was 42.9 ± 0.86 years (women 43.6 ± 0.93 years, men 39 ± 2.29 years) (Table 1).

Only patients diagnosed with Graves' disease were included in the study. Exclusion criteria were toxic adenoma, multinodular toxic goiter, autoimmune thyroiditis in the phase of thyrotoxicosis. Patients with different severity of thyrotoxicosis were included in the study.

Table 2. Hormonal changes of thyroid hormones in the examined patients.

Nosology of thyroid pathology	Control group n-10	DTG, subclinical thyrotoxicosis n-35	DTG, manifest thyrotoxicosis n-22
TSH, mEd/l	$2,2 \pm 0,7$	$0,16 \pm 0,07^*$	$0,13 \pm 0,02^*$
fr.T3, pg/mL	$2,8 \pm 0,3$	$3,8 \pm 0,5^*$	$8,8 \pm 1,1^*$
fr.T4, pg/mL	$14,2 \pm 1,9$	$15,7 \pm 2,1^*$	$26,9 \pm 2,3^*$
TRAb, IU/l	$0,3 \pm 0,02$	$7,4 \pm 0,9^*$	$9,4 \pm 1,5^*$
TPOAb, IU/l	$14,6 \pm 3,4$	$67,4 \pm 8,5^*$	$98,7 \pm 9,1^*$

Note. Significance of difference to CG: * $P < 0.05$ in relation to CG.

According to the results of hormonal background, the patients with Graves' disease were divided into 2 groups: 22 patients with manifest form of thyrotoxicosis (38,4%) and 35 patients with subclinical form (61,6%).

Thus, in the group with SG the content of fr.T3 was increased by 27% ($P < 0.05$), fr.T4 was comparable to the control group, against the background of decreased TTG. The rise of TRAb and TPOAb was noted. In the group with MG, fr.T3 increased by 69% ($P < 0.05$), fr.T4 - by 49% ($P < 0.05$) against the background of high values of TRAb and TPOAb.

Subclinical thyrotoxicosis is characterized by elevated levels of TSH with normal thyroid hormones values and mild clinical symptoms, while the manifest form is characterized by a pronounced clinic and elevated levels of thyroid hormones and decreased TSH typical for this form of thyrotoxicosis [3,6,15,16]. When analyzing the hormonal spectrum of patients, it was revealed that TSH was decreased in all groups and there was a rise in fr.T3 and fr.T4 in the group with manifest thyrotoxicosis, indicating thyroid hyperfunction. Immunologic markers, TRAb and TPOAb are also elevated, which confirms the autoimmune nature of the diseases.

Table 3. Thyroid volume in the studied patients.

	Control, n-10	DTG, subclinical thyrotoxicosis n-35	DTG, manifest thyrotoxicosis n-22
Thyroid volume, ml	16,47±4,7	37,66±5,5*	39,3±2,3*

Note. Reliability of difference to CG: * P<0.05 in relation to CG.

As can be seen from Table 3, in patients with DTG, the volume of the thyroid is increased both in the group with manifest and subclinical thyrotoxicosis, relative to the control group.

The main clinically most significant causes of thyrotoxicosis in the region of iodine deficiency are DTG, which, in turn, in most cases is manifested by diffuse or multinodular toxic goiter. If toxic adenoma by pathogenesis is an iodine-deficient disease that develops as a result of chronic, ongoing for many years thyroid hyperstimulation, DTG is a systemic autoimmune disease, the basis of the pathogenesis of which is the production of stimulating antibodies to the thyroid hormone receptor (TRAb).

It should be emphasized that the most significant predictor of the development of complications of DTG is the duration of the disease. In this regard, early diagnosis of thyrotoxicosis and adequate treatment can prevent the development of rhythm disturbances and cardiovascular insufficiency, when the risk of such complications is the highest [7,21,23,26]. Depending on the duration of the disease, patients were divided into 3 groups: 1-group - up to 1 year, 2-group - 1-4 years, 3-group - more than 4 years.

Table 4. Development of complications in Graves' disease patients depending on the duration of the disease

Groups	Thyrotoxic heart	Graves' ophthalmopathy	Toxic hepatitis	TSH, IU/L
1 group, n-23	3 (13,0%)	7 (30,4%)	-	0,21±0,01
2 group, n-19	5 (26,3%)	14 (73,6%)	4 (21,0%)	0,12±0,06
3 group, n-15	8 (53,3%)	13 (68,4%)	6 (37,5%)	0,23±0,09

Such complications as thyrotoxic heart were observed in 3 (13.0%) patients, Graves' ophthalmopathy in 7 (30.4%) patients in group 1, in group 2 in 5 (26.3%) and 14 (73.6%); in group 3 in 8 (53.3%) and 13 (68.4%) patients, respectively. Toxic hepatitis was not detected in group 1, in group 2 in 21.0%, and in group 3 in 37.5% of cases (Table 4). As can be seen from the table, there is an increase in complications such as thyrotoxic heart, endocrine ophthalmopathy and toxic hepatitis with the duration of the disease. According to the literature, as a result of sympathomimetic action of thyroid hormones, the functional activity of all organs and systems of the body increases, and the most

characteristic changes are observed in the nervous system (increased excitability, irritability, trembling, sweating), cardiovascular system (tachycardia, increased pulse pressure, atrial fibrillation) and gastrointestinal tract (increased motor function, weight loss with increased appetite) [20], [21].

In group 1, where patients received thyrotropics in a daily dose of 25.4 ± 2.1 mg/day (mean TSH level 0.21 ± 0.01 MEd/l), in group 2 patients took thyrotropics in a daily dose of 15.1 ± 1.6 mg/day (mean TSH level 0.12 ± 0.04 MEd/l), in group 3 - 12.2 ± 5.1 mg/day (mean TSH level 0.23 ± 0.09 MEd/l). As can be seen, with the duration of the disease there is a decrease in the dose of thyrostatics, but there is no clinical improvement. In patients who achieved clinical improvement the average level of TSH amounted to 1.2 ± 0.05 IU/l. The majority of patients received inadequate doses of thyrostatics and were in decompensation stage despite the terms of the disease [22], [23], [24], [25].

Patients were prescribed adequate doses of thyrostatics and B-adrenoblockers during 3 months. In the presence of complications from the cardiovascular system, the patients were consulted by a cardiologist and the necessary recommendations were given [26], [27]. After improvement of general condition and hormonal remission 35 (32.7%) patients were referred to surgeons to solve the problem by radical method - thyroidectomy [28]. Among 57 patients, 39 (68.4%) patients achieved clinical and hormonal remission and continued drug therapy. 18 (31.6%) patients were sent for consultation to surgeons for thyroidectomy, after achieving euthyroidism by medication, due to large thyroid volume. 16 (28.0%) patients were added glucocorticosteroids because of the severity of endocrine ophthalmopathy. The SF-36 questionnaire was used to study the QOL of patients with DTG depending on the therapy received. All patients with DTG were divided into 2 groups. The first group consisted of 39 patients with DTG who received drug therapy and improved clinical and hormonal parameters and the second group consisted of 18 patients after thyroidectomy for DTG. The following early and late postoperative complications were observed in 18 operated patients: 3 (16,5%) patients developed transient hypoparathyroidism immediately after total thyroidectomy and the condition recovered after vitamin D and calcium preparations addition; 1 (5,5%) patient developed vocal cord paresis. These patients were followed up with an endocrinologist and otorhinolaryngologist to rehabilitate the complications present. These patients were not included in this group. In the patients of both groups, all the parameters of QoL at examination were significantly lower than in healthy individuals ($P < 0.001$) for all scales in group 1: $P < 0.01$ for the vitality scale in group 2 and $P < 0.001$ for all other parameters in group 2 (Table 5). There were the following differences between the patients of the two groups: parameters of physical functioning, vitality, social, emotional functioning and psychological health were significantly higher in the group of patients after total and subtotal thyroidectomy ($P < 0,001$), parameters of role functioning did not differ significantly in both groups of patients, and parameters of social functioning were significantly higher (by 30,7%) in the group of patients receiving drug therapy with thyrostatics ($P < 0,001$). When comparing the QOL of patients with DTC in both groups, it

turned out that the mean values of physical functioning, role physical functioning, social functioning, role emotional functioning and mental health after surgery were significantly higher than those of patients receiving drug therapy with thyrostatics, although in both groups the mean TSH level did not differ significantly. In the first group the mean TSH level was 2.3 ± 0.02 IU/L, in the second group 3.1 ± 0.05 IU/L. Emotional functioning and psychological health were higher in group 2 patients by 40.7% and 22.5%, respectively.

Table 5. Parameters for assessing the quality of life in patients with DTG depending on therapy

Parameters	CG, n-10	1 group, n-39	2 group, n-18
Physical functioning	71,30 $\pm$ 3,01	44,13 $\pm$ 7,08*,***	48,33 $\pm$ 5,38***^
Role functioning	87,342 $\pm$ 11,28	60,10 $\pm$ 9,24*,***	74,14 $\pm$ 10,62***
Pain	11,16 $\pm$ 3,74	21,13 $\pm$ 9,41***	16,32 $\pm$ 9,72***
General health	76,17 $\pm$ 7,26	56,23 $\pm$ 9,33***	65,02 $\pm$ 9,14
Vitality	77,06 $\pm$ 9,76	51,50 $\pm$ 6,11*,***	54,25 $\pm$ 4,22*,***^
Social functioning	81,13 $\pm$ 7,84	69,33 $\pm$ 7,59*,***	73,95 $\pm$ 9,02***
Emotional functioning	82,57 $\pm$ 8,41	63,53 $\pm$ 9,70***	68,81 $\pm$ 8,97***^
Psychological health	83,65 $\pm$ 5,57	54,27 $\pm$ 8,95***	70,28 $\pm$ 8,64^

Note. Reliability of difference with CG: **P<0.01, ***P<0.001; reliability of difference between groups 1 and 2: ^P<0.05 CG- control group

Thus, timely referral for thyroidectomy for DTG in dynamics leads to improvement of patients' QOL. After thyroidectomy all patients should undergo hormonal examination with the purpose of timely DHT. Timely administration of antithyroid drugs improves QOL and prevents the development of complications from various organs and systems.

CONCLUSION

Fundamental Finding : Women are more frequently affected by DTG than men, with a 2:1 ratio. Among patients, subclinical thyrotoxicosis is more common (66.7%) than manifest thyrotoxicosis (33.3%). Both groups exhibit significantly elevated antibody levels to TS receptors, indicating a common immunological mechanism in disease progression. **Implication :** The study highlights the critical impact of disease duration on DTG complications, including thyrotoxic heart, endocrine ophthalmopathy, and toxic hepatitis. This finding suggests that early diagnosis and management are essential to mitigate severe outcomes, emphasizing the need for timely intervention strategies in clinical practice. **Limitation :** This study primarily focuses on the relationship between disease duration and complications without considering other potential influencing factors, such as genetic predisposition or environmental triggers. Additionally, the

sample size and demographic diversity were not extensively analyzed, limiting the generalizability of the findings. **Future Research** : Future studies should explore additional risk factors contributing to DTG complications, including genetic, environmental, and lifestyle influences. Comparative analysis between different treatment modalities, including long-term follow-up of surgical and drug therapies, would provide deeper insights into optimizing patient outcomes.

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